REMARKS

Claims 1-5, 8-10 and 16-18 are pending. Claims 1-5, 8-10 and 16-18 were rejected. By virtue of this response, claim 2 has been cancelled, and claim 1, 3, and 4 have been amended. Accordingly, claims 1, 3-5, 8-10, and 16-18 are currently under consideration. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any subject matter of the claims previously presented.

Amendments to the Claims

Claim 1, 3, and 4 have been amended. Support the amendment of claim 1 may be found, for example, on page 17, lines 17-19; page 30, line 23 – page 31, line 2, page 34, lines 16-18 and 20-21; and previously pending claim 2.

With respect to all amendments to the claims, Applicant has not dedicated or abandoned any unclaimed subject matter, and moreover, have not acquiesced to any rejections and/or objections made by the Office. Applicant expressly reserves the right to pursue prosecution of presently excluded claim embodiments in future continuation, continuation-in-part, and/or divisional applications.

For the Examiner's convenience, Applicant's remarks are presented in the same order in which they were raised in the Office Action.

Claim Rejections – 35 USC § 112

The Applicant acknowledges the withdrawal of the rejection of claims of claims 1-5, 8-10, and 16-18 under 35 U.S.C. § 112, first paragraph, as failing to comply with the [full scope] enablement requirement.

Claim Rejections – 35 USC § 112

Claims 1, 3-5, 8-10, and 16-18 remain rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement.

Applicant respectfully traverses this rejection. The specification provides adequate guidance to enable claims 1, 3-5, 8-10, and 16-18 in accordance with 35 U.S.C. § 112, first

paragraph. The Examiner alleges at page 3 of the Office Action that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertain, or with which it is most nearly connected, to make and/or use the invention.

II. The Examiner alleges that undue experimentation is required of the skilled artisan to practice the invention. Applicant respectfully traverses. The claims, as amended, recite a "method of suppressing a respiratory syncytial virus (RSV) infection in an individual who is at risk of being exposed to RSV, comprising administering a composition to the respiratory tract of said individual by local administration, said composition comprising a polynucleotide comprising an immunostimulatory sequence (ISS) to said individual, wherein the ISS comprises the sequence 5'-T,C,G-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length, … wherein said composition is administered between about 3 days and about 14 days before exposure to RSV, and wherein said composition is administered in an amount sufficient to suppress an RSV infection."

At page 17, lines 17-19 and page 17, line 26 - page 18, line 8, the specification teaches structural and sequence characteristics of an ISS comprising the sequence 5'-T,C,G-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length. The specification states that "ISS have been described in the art and may be readily identified using standard assays which indicate various aspects of the immune response, such as cytokine secretion, antibody production, NK cell activation and T cell proliferation." Page 17, lines 3-10. The specification provides a number of references that describe ISS. See pages 3-4.

On page 17, lines 11-15, the specification teaches that "[t]he ISS can be of any length greater than 6 bases or base pairs and generally comprises the sequence 5'-cytosine, guanine-3', preferably greater than 15 bases or base pairs, more preferably greater than 20 bases or base pairs in length." The specification teaches that an ISS may comprise (i.e., contain one or more of) the sequence 5'-T, C, G-3'. See page 17, line 17-19. The specification also teaches that in some embodiments, an ISS may comprise the sequence 5'-C, G, pyrimidine, pyrimidine, C, G-3' (such as 5'-CGTTCG-3'). See page 17, line 19-20. The specification also teaches that in some embodiments, an ISS may comprise the sequence 5'-C, G, pyrimidine, pyrimidine, C, G, purine, purine-3'. See

page 17, line 20-22. The specification also teaches that in some embodiments, an ISS may comprise the sequence 5'-purine, T, C, G, pyrimidine, pyrimidine-3'. See page 17, line 24-25. Furthermore, the specification teaches approximately 160 specific ISSs. See page 18, line 9 through page 20, lines 2.

Further, the specification teaches an assay to determine whether an ISS is administered in an amount sufficient to suppress an RSV infection. The specification discloses several methods for assessing suppression of RSV infection. The specification teaches that "[r]hinitis, nasal mucous production, severity of cough, myalgia, elevated body temperature, and other symptoms of respiratory virus infection may be easily measured using simple tests and/or scales as are known in the art. Viral titer may be assessed in biological samples using standard methods known in the art." Page 35, lines 10-15. In addition, Example 2 teaches that administration of an immunostimulatory sequence (ISS) to an individual "before infection … was effective at reducing viral titers." See page 40, lines 9-10.

The specification teaches sequence requirements for ISSs, provides specific examples of ISSs, and provides information regarding how to identify and evaluate other ISSs using techniques known in the art. Based on the teaching of the specification, a person of ordinary skill in the art would be able to practice the claimed invention without undue experimentation.

The Examiner at page 5 further states that the application has shown that the administration of an illustrative ISS, that is, the ISS shown in SEQ ID NO:1, was the only sequence used in working examples. The Examiner at page 13 additionally states that the application does not offer guidance in the specification concerning the effective use of oligonucleotide containing CpG motif to suppress RSV infection in an individual. Applicant respectfully traverses.

First, a specific level of suppression of an RSV infection, or clinical efficacy sufficient to suppress an RSV infection, is not required for compliance with the enablement requirement of Section 112, first paragraph, as relates to the claims. The presently amended claims merely require that the "composition is administered in an amount sufficient to suppress an RSV infection."

Secondly, the specification demonstrates that a sequence comprising the ISS recited in claim 1 and 5 and one of the ISS sequences recited in claim 3 and claim 4 is effective in the animal

models disclosed in the Examples. SEQ ID NO:1, which was used in Example 2 is comprised of the sequence recited in Claim 1, that is 5'-T, C,G -3' (SEQ ID NO:1: 5'-TGACTGTGAACGTTCGAGATGA-3'); comprises one of the sequences recited in claim 3, that is 5'-purine, purine, C, G, pyrimidine, pyrimidine, C, G-3' (SEQ ID NO:1: 5'-TGACTGTGAACGTTCGAGATGA-3'); comprises the sequence recited in Claim 4, that is 5'-AACGTTCG-3' and 5'-GACGTTCG-3 (SEQ ID NO:1: 5'-TGACTGTGAACGTTCGAGATGA-3'); and comprises the sequence recited in claim 5, that is 5'-TGACTGTGAACGTTCGAGATGA-3' (SEQ ID NO:1).

The Examiner references Infante-Durante et al. as teaching the need for a balance between Th1 and Th2 type immune responses. The Examiner also references Aoki et al., Bohn et al., Sakao et al., Zaitseva et al., and Masihi, K. as teaching that Th1 associated cytokines have different levels of efficacy against intracellular pathogens. The Applicant respectfully notes that the currently pending claims recite a method of suppressing a RSV infection using an ISS; none of these references discuss RSV.

The Examiner further states Yamamoto et al., Equils et al., Agrawal et al., and Olbrich et al. evidence the challenges in harnessing the immunostimulatory activity of oligonucleotides containing the CpG motif to trigger an innate immune response. The Applicant respectfully notes that the currently pending claims recite a method of suppressing a RSV infection; none of these references discuss using an ISS to suppress a RSV infection.

The Examiner further states that Krieg et al. and Mutwiri et al. teach that the Th1 associated cytokine profiles for oligonucleotides vary from one oligonucleotide and species of subject to the next. The Examiner states that Krieg et al. "notes that each oligonucleotide containing the CpG motif must be considered as a separate agent…" Office Action at page 7. Krieg et al on page 714, first full paragraph states that "[i]n general CpG DNA stimulates B cells, NK cells, CD, and monocytes/macrophages, regardless of whether the DNA is in the form of genomic bDNA or in the form of synthetic ODN with a nuclease-resistant PS backbone." Krieg et al. states in the paragraph that bridges pages 716-717, in particular, that "Even though PS ODN as a family have

similar properties, there are still qualitative differences in their effects…. To some degree then, every DNA molecule containing CpG motifs must be considered as a separate agent."

Krieg et al. indicates that DNA molecules containing CpG motifs are a family with similar properties while acknowledging that to some extent, there is variation within the family as to qualitative differences.

The Examiner cites Mutwiri et al. as teaching that "the immunostimulatory activity of oligonucleotides containing the CpG is very species specific, as evidenced by Mutwiri et al." Office Action at page 8. Mutwiri states on page 90 starting at the bottom of the column that "[e]arly studies indicated that cells from several mammalian species may be stimulated by synthetic ODN containing different CpG motifs, and the terms mouse (GACGTT) and human (GTCGTT) motif were adopted despite the act that the human motif also had some stimulatory effects in mice." Thus, contrary to the Examiner's assertion, not all ISS immunostimulatory activity is species specific. Further, Mutwiri on page 90 in the second column indicates that "[t]ogether, these data suggest that in vitro stimulation of cells by CpG motifs is conserved across species, and the enhanced activity of the GACGTT motif in laboratory animals may be an artificial bias due to inbreeding" (emphasis added).

In addition, the Applicant respectfully disagrees with the assertion that "Table 1 of Mutwiri et al. provides that the *in vitro* immunostimulatory activity of oligonucletides containing the CpG motif varies from one species to the next." Applicants respectfully note in Table 1 on page 92 of Mutwiri et al. "empty spaces indicate parameter was not tested." When evaluating TNF-α activity of CpG ODN in vitro cattle, there was +/- activity. Excluding the +/- result, in no case in Table 1 at page 92 of Mutwiri et al., was there an in vitro activity of CpG ODN tested in a species which resulted in a differential species effect on immune response.

The claimed invention is enabled if one of skill in the art can make and use the claimed invention based on the disclosure in the specification coupled with knowledge known in the art, without resorting to undue experimentation. Different ISSs may have different levels of immunostimulatory activities based on flanking sequences or in different species of mammals.

However, Applicant notes that compliance with Section 112, first paragraph does not require optimizing ISS sequences.

As the court held in In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988), the test for enablement does not rest merely on the quantity of experimentation that would be required to practice an invention, "since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." Contrary to the Examiner's assertion, the quantity of experimentation is not a criterion for undue experimentation.

Applicant submits that the disclosure of specific ISS sequences that "comprises the sequence 5'-T,C,G-3', wherein the polynucleotide is greater than 6 and less than about 200 nucleotides in length," wherein the ISS "is administered in an amount sufficient to suppress an RSV infection," disclosure of methods for assessing suppression of RSV, and examples of suppression of RSV when the ISS are locally administered to the respiratory tract of an individual at risk of being exposed to RSV between about 3 and about 14 days, enable one of skill in the art to make and use the claimed invention without resorting to undue experimentation.

Therefore, Applicant submits that claims 1, 3-5, 8-10 and 16-17 enabled in accordance with 35 U.S.C. § 112, first paragraph and request withdrawal of this ground for rejection.

Double Patenting

Claims 1, 3-5, 8-10 and 16-17 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 11 of copending Application No. 10/898,512. When the conflicting claims have been found to be allowable, Applicant will address this provisional double patenting rejection with a terminal disclaimer.

Claims 1, 3-5, 8-10 and 16-17 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application No. 10/426,237. When the conflicting claims have been found to be allowable, Applicant will address this provisional double patenting rejection with a terminal disclaimer.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 377882000900. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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